Efforts will be made by the Joint Sectoral Committee to reach unanimous consent on the appropriate action. If agreement to suspend is reached in the Joint Sectoral Committee, an authority may be suspended immediately thereafter. If no agreement is reached in the Joint Sectoral Committee, the matter is referred to the Joint Committee. If no unanimous consent is reached within 30 days after such notification, the contested authority will be suspended.

Upon the suspension of an authority previously listed as equivalent, a Party is no longer obligated to normally endorse the inspection reports of the suspended authority. A Party shall continue to normally endorse the inspection reports of that authority prior to suspension, unless the authority of the receiving party decides otherwise based on health or safety considerations. The suspension will remain in effect until unanimous consent has been reached by the Parties on the future status of that authority.

U.S. - EC MRA Pharmaceutical Good Manufacturing Practices Annex

CHAPTER 5

JOINT SECTORAL COMMITTEE

Article 17

Role and composition of the Joint Sectoral Committee

A Joint Sectoral Committee is set up to monitor the activities under both the transitional and operational phases of this Annex.

The Committee will be co-chaired by a representative of FDA for the U.S. and a representative of the EC who each will have one vote. Decisions will be taken by unanimous consent.

The Joint Sectoral Committee's functions will include:

1. making a joint assessment, which must be agreed by both Parties, of the equivalence of the respective authorities,

2. developing and maintaining the list of equivalent authorities, including any limitation in terms of inspecting type or products, and communicating the list to all authorities and the Joint Committee,

3. providing a forum to discuss issues relating to this Annex, including concerns that an authority may be no longer equivalent and opportunity to review product coverage,

4. consideration of the issue of suspension.

The Joint Sectoral Committee shall meet at the request of either Party and, unless the co-chairs otherwise agree, at least once each year. The Joint Committee will be kept informed of the agenda and conclusions of meetings of the Joint Sectoral Committee.

CHAPTER 6

INFORMATION EXCHANGE

Article 18

Regulatory collaboration

The Parties and authorities shall inform and consult one another, as permitted by law, on proposals to introduce new controls or to change existing technical regulations or inspection procedures and to provide the opportunity to comment on such proposals.

The Parties shall notify each other in writing of any changes to Appendix 2.

Article 19

Information relating to quality aspects

The authorities will establish an appropriate means of exchanging information on any confirmed problem reports, corrective actions, recalls, rejected import consignments and other regulatory and enforcement problems for products subject to this Annex.

Article 20

Alert System

The details of an alert system will be developed during the transitional period. The system will be maintained in place at all times. Elements to be considered in developing such a system are described in Appendix 5.

Contact points will be agreed between both Parties to permit authorities to be made aware with the appropriate speed in case of quality defect, recalls, counterfeiting and other

problems concerning quality, which could necessitate additional controls or suspension of the distribution of the product.

CHAPTER 7

SAFEGUARD CLAUSE

Article 21

Each Party recognizes that the importing country has a right to fulfil its legal responsibilities by taking actions necessary to ensure the protection of human and animal health at the level of protection it deems appropriate. This includes the suspension of the distribution, product detention at the border of the importing country, withdrawal of the batches and any request for additional information or inspection as provided in Article 12.

APPENDIX 1

List of applicable laws, regulations and administrative provisions

For the European Community:

Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, as extended, widened and amended.

Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, as extended, widened and amended.

Council Directive 81/851/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products, as widened and amended.

Commission Directive 91/356/EEC of 13 June 1991 laying down the principles and guidelines of good manufacturing practice for medicinal products for human use.

Commission Directive 91/412/EEC of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products.

Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products.

Council Directive 92/25/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use.

Guide to Good Distribution Practice (94/C 63/03).

Current version of the Guide to Good Manufacturing Practice, Rules Governing Medicinal Products in the European Community, Volume IV.

For the United States:

Relevant sections of the United States Federal Food, Drug, and Cosmetic Act and the United States Public Health Service Act.

Relevant sections of Title 21, United States Code of Federal Regulations (CFR) Parts 1-99, Parts 200-299, Parts 500-599, and Parts 600-799.

Relevant sections of the FDA Investigations Operations Manual, the FDA Regulatory Procedures Manual, the FDA Compliance Policy Guidance Manual, the FDA Compliance Program Guidance Manual, and other FDA guidances.

APPENDIX 2

List of Authorities

United States:

In the United States, the regulatory authority is the Food and Drug Administration.

European Community:

In the European Community, the regulatory authorities are the following:

BELGIUM	Inspection générale de la Pharmacie Algemene Farmaceutische Inspectie
DENMARK	Laegemiddelstyrelsen
GERMANY	Bundesministerium für Gesundheit for immunologicals: Paul-Ehrlich-Institut, Federal Agency for Sera & Vaccines
GREECE	Εθνικός Οργανισμός Φαρμάκου Ministry of Health and Welfare National Drug Organization (E.O.F.)
SPAIN	for medicinal products for human use: Ministerio de Sanidad y Consumo Subdirección General de Control Farmacéutico for medicinal products for veterinary use: Ministerio de Agricultura, Pesca y Alimentación (MAPA) Dirección General de la Producción Agraria

FRANCE	for medicinal products for human use: Agence du Médicament for veterinary medicinal products: Agence Nationale du Médicament Vétérinaire
IRELAND	Irish Medicines Board
ITALY	for medicinal products for human use: Ministero della Sanità Dipartimento Farmaci e Farmacovigilanza for medicinal products for veterinary use: Ministero della Sanità Dipartimento alimenti e nutrizione e sanità pubblica veterinaria – Div. IX
LUXEMBOURG	Division de la Pharmacie et des Médicaments
NETHERLANDS	De Minister van Volksgezondheid, Welzijn, en Sport Inspectie voor de Gezondheidszorg
AUSTRIA	Bundesministerium für Arbeit, Gesundheit und Soziales
PORTUGAL	Instituto da Farmácia e do Medicamento – INFARMED
FINLAND	Lääkelaitos/Läkemedelsverket (National Agency for Medicines)
SWEDEN	Läkemedelsverket – Medical Products Agency
UNITED KINGDOM	for human and veterinary (non-immunologicals):

Medicines Control Agency

for veterinary immunologicals:
Veterinary Medicines Directorate

EUROPEAN COMMUNITY Commission of the European Communities
European Agency for the Evaluation of Medicinal Products (EMEA)

APPENDIX 3

Indicative list of Products covered by the Sectoral Annex

Recognizing that precise definition of medicinal products and drugs are to be found in the legislation referred to above, an indicative list of products covered by the agreement is given below:

- human medicinal products including prescription and non-prescription drugs;

- human biologicals including vaccines, and immunologicals;

- veterinary pharmaceuticals, including prescription and non-prescription drugs, with the exclusion of veterinary immunologicals;

- pre-mixes for the preparation of veterinary medicated feeds (EC), Type A medicated articles for the preparation of veterinary medicated feeds (US);

- intermediate products and active pharmaceutical ingredients or bulk pharmaceuticals (US)/starting materials (EC).

APPENDIX 4

Criteria for Assessing Equivalence for Post- and Pre-Approval

I. Legal/Regulatory authority and structures and procedures providing for post- and pre-approval:

A. Appropriate statutory mandate and jurisdiction.

B. Ability to issue and update binding requirements on GMPs and guidance documents.

C. Authority to make inspections, review and copy documents, and to take samples and collect other evidence.

D. Ability to enforce requirements and to remove products found in violation of such requirements from the market.

E. Substantive current good manufacturing requirements.

F. Accountability of the regulatory authority.

G. Inventory of current products and manufacturers.

H. System for maintaining or accessing inspection reports, samples and other analytical data, and other firm/product information relating to matters covered by this Sectoral Annex.

II. Mechanisms in place to assure appropriate professional standards and avoidance of conflicts of interest.

III. Administration of the regulatory authority:

A. Standards of education/qualification and training.

B. Effective quality assurance systems measures to ensure adequate job performance.

C. Appropriate staffing and resources to enforce laws and regulations.

IV. Conduct of Inspections:

A. Adequate pre-inspection preparation, including appropriate expertise of investigator/team, review of firm/product and databases, and availability of appropriate inspection equipment.

B. Adequate conduct of inspection, including statutory access to facilities, effective response to refusals, depth and competence of evaluation of operations, systems and documentation; collection of evidence; appropriate duration of inspection and completeness of written report of observations to firm management.

C. Adequate post-inspection activities, including completeness of inspectors' report, inspection report review where appropriate, and conduct of follow-up inspections and other activities where appropriate, assurance of preservation and retrieval of records.

V. Execution of regulatory enforcement actions to achieve corrections, designed to prevent future violations, and to remove products found in violation of requirements from the market.

VI. Effective Use of Surveillance Systems:

A. Sampling and analysis.

B. Recall monitoring.

C. Product defect reporting system.

D. Routine surveillance inspections.

E. Verification of approved manufacturing process changes to marketing authorizations/approved applications.

VII. Additional specific criteria for pre-approval inspections

A. Satisfactory demonstration through a jointly developed and administered training program and joint inspections to assess the authorities' capabilities.

B. Pre-inspection preparation includes the review of appropriate records, including site plans and drug master file or similar documentation to enable adequate inspections.

C. Ability to verify chemistry, manufacturing and control data supporting an application is authentic and complete.

D. Ability to assess and evaluate research and development data as scientifically sound, especially transfer technology of pilot, scale up and full scale production batches.

E. Ability to verify conformity of the on site processes and procedures with those described in the application.

F. Review and evaluate equipment installation, operational and performance qualification data, and evaluate test method validation.

APPENDIX 5

Elements to be Considered in Developing a Two-way Alert System

1. Documentation

   - Definition of a crisis/emergency and under what circumstances an alert is required
   - Standard Operating Procedures (SOPs)
   - Mechanism of health hazards evaluation and classification
   - Language of communication and transmission of information

2. Crisis Management System

   - Crisis analysis and communication mechanisms
   - Establishment of contact points
   - Reporting mechanisms

3. Enforcement Procedures

   - Follow-up mechanisms
   - Corrective action procedures

4. Quality Assurance System

   - Pharmacovigilance programme
   - Surveillance/monitoring of implementation of corrective action

5. Contact points

   For the purpose of this agreement, the contact points for the alert system will be:

for the European Community:
the Executive Director of the European Agency for the Evaluation of Medicinal Products, 7, Westferry Circus, Canary Wharf, UK – London E14 4HB, England.
Telephone +44-171-418 8400, Fax 418 8416.

for the United States:
(to be provided by the U.S.)

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U.S. - EC MRA Medical Devices Annex

SECTORAL ANNEX ON

MEDICAL DEVICES

PREAMBLE

This Annex constitutes a Sectoral Annex to the Agreement on Mutual Recognition in Relation to Conformity Assessment between the United States and the European Community.

Carrying out the provisions of this Annex will further public health protection, will be an important means of facilitating commerce in medical devices and will lead to reduced costs for regulators and manufacturers of both Parties.

U.S. - EC MRA Medical Devices Annex

CHAPTER 1

PURPOSE, SCOPE AND COVERAGE OF THE SECTORAL ANNEX

Article 1

Purpose

1. The purpose of this Annex is to specify the conditions under which a Party will accept the results of quality system-related evaluations and inspections and premarket evaluations of the other Party with regard to medical devices as conducted by listed conformity assessment bodies (CABs) and to provide for other related cooperative activities.

2. This Annex is intended to evolve as programmes and policies of the Parties evolve. The Parties will review this Annex periodically, in order to assess progress and identify potential enhancements to this Annex as Food and Drug Administration (FDA) and EC policies evolve over time.

Article 2

Scope

1. The provisions of this Annex shall apply to the exchange and, where appropriate, endorsement of the following types of reports from CABs assessed to be equivalent:

   (a) Under the U.S. system, surveillance/post-market and initial/pre-approval inspection reports;

   (b) Under the U.S. system, premarket (510(k)) product evaluation reports;

   (c) Under the EC system, quality system evaluation reports; and

   (d) Under the EC system, EC type examination and verification reports.

   Appendix 1 names the legislation, regulations, and related procedures under which:

   (a) products are regulated as medical devices by each Party;

   (b) CABs are designated and confirmed; and

   (c) these reports are prepared.

2. For purposes of this Annex, equivalence means that: CABs in the EC are capable of conducting product and quality systems evaluations against U.S. regulatory requirements in a manner equivalent to those conducted by FDA; and CABs in the U.S. are capable of conducting product and quality systems evaluations against EC regulatory requirements in a manner equivalent to those conducted by EC CABs.

Article 3

Product Coverage

There are three components to this agreement each covering a discrete range of products:

1. Quality System Evaluations – U.S.-type surveillance/post-market and initial/pre-approval inspection reports and EC-type quality system evaluation reports will be exchanged with regard to all products regulated under both U.S. and EC law as medical devices.

2. Product Evaluation – U.S.-type premarket (510(k)) product evaluation reports and EC-type-testing reports will be exchanged only with regard to those products classified under the U.S. system as Class I/Class II – Tier 2 medical devices which are listed in Appendix 2.

3. Post-Market Vigilance Reports – Post-market vigilance reports will be exchanged with regard to all products regulated under both U.S. and EC law as medical devices.

Additional products and procedures may be made subject to this Annex by agreement of the Parties.

Article 4

Regulatory Authorities

The regulatory authorities shall have the responsibility of implementing the provisions of this Annex, including the designation and monitoring of CABs. Regulatory authorities are specified in Appendix 3. Each Party will promptly notify the other Party in writing of any change in the regulatory authority for a country.

CHAPTER 2

TRANSITION PERIOD

Article 5

Length and purpose of transition period

There will be a three-year transition period immediately following the date of entry into force of the Agreement. During the transition period, the Parties will engage in confidence-building activities for the purpose of obtaining sufficient evidence to make determinations concerning the equivalence of CABs of the other Party with respect to the ability to perform quality system and product evaluations or other reviews resulting in reports to be exchanged under this Annex.

Article 6

Listing of CABs

Each Party shall designate CABs to participate in confidence-building activities by transmitting to the other Party a list of CABs which meet the criteria for technical competence and independence, as identified in Appendix 1. The list shall be accompanied by supporting evidence. Designated CABs will be listed in Appendix 4 for participation in the confidence building activities once confirmed by the importing Party.
Non-confirmation would have to be justified based on documented evidence.

Article 7

Confidence Building Activities

1. At the beginning of the transitional period, the Joint Sectoral Group will establish a joint confidence building programme calculated to provide sufficient evidence of the capabilities of the designated CABs to perform quality system or product evaluations to the specifications of the Parties.

2. The joint confidence building program should include the following actions and activities:

   (a) Seminars designed to inform the Parties and CABs about each Party's regulatory system, procedures, and requirements;

   (b) Workshops designed to provide the Parties with information regarding requirements and procedures for the designation and surveillance of CABs;

   (c) Exchange of information about reports prepared during the transition period;

   (d) Joint training exercises; and

   (e) Observed inspections.

3. During the transition period, any significant problem that is identified with a CAB may be the subject of cooperative activities, as resources allow and as agreed to by the regulatory authorities, aimed at resolving the problem.

4. Both Parties will exercise good faith efforts to complete the confidence building activities as expeditiously as possible to the extent that the resources of the Parties allow.

5. Both the EC and the U.S. will each prepare annual progress reports which will describe the confidence building activities undertaken during each year of the transition period. The form and content of the reports will be determined by the Parties through the Joint Sectoral Committee.

Article 8

Other transition period activities

1. During the transition period, the Parties will jointly determine the necessary information which must be present in quality system and product evaluation reports.

2. The Parties will jointly develop a notification and alert system to be used in case of defects, recalls, and other problems concerning product quality that could necessitate additional actions (e.g., inspections by the Parties of the importing country) or suspension of the distribution of the product.